



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

~~MAR 24 1985~~

SUBJECT: EPA File Symbol 100-ALI
Ridomil/Bravo 81W Fungicide

FROM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

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TO: Henry Jacoby, PM 21
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APPLICANT: Agricultural Division
Ciba-Geigy Corporation
P.O. Box 18300
Greensboro, NC 27419

ACTIVE INGREDIENTS:

275HA Metalaxyl: N-(2,6-dimethylphenyl)-N-(methoxyacetyl)
alanine methyl ester 9.0%
215B Chlorothalonil: Tetrachloroisophthalonitrile . . 72.0%
INERT INGREDIENTS: 19.0%

BACKGROUND:

The applicant has submitted an acute oral, acute dermal, acute inhalation, primary eye irritation, primary skin irritation, and dermal sensitization studies. The studies were conducted by Ciba-Geigy Pharmaceuticals Division. The data Accession Number is 257976. The method of support is owner submission.

RECOMMENDATION:

FHB/TSS finds all the studies acceptable to support registration of 100-ALI. The signal word is "DANGER" based on the primary eye irritation study.

10/7

LABELING:

1. Revise the precautionary statements to include the following:

Wear a mask or pesticide respirator jointly approved by the Mining Enforcement and Safety Administration and the National Institute for Occupational Safety and Health.

2. The precautionary statements should precede the Directions for Use.
3. The Conditions of Sale and Warranty should appear at the end of the Directions for Use.
4. The following information must appear directly under the heading "Directions For Use:"
 - a. "It is a violation of Federal law to use this product in a manner inconsistent with its labeling."
 - b. The subheading "Reentry Statements" and information.

REVIEW:

- (1) Acute Oral Toxicity Study: Ciba-Geigy Pharmaceuticals Division; Report No. 295-84; January 23, 1985.

PROCEDURE:

Five male and five female rats were administered a single oral dose of 5000 mg/kg of test material suspended in 3 percent cornstarch. Additional groups of five females were also dosed at the following levels: 500, 750, 1000, 2500, or 3750 mg/kg. Animals were observed frequently on day of dosing and twice daily on days 2 to 14.

RESULTS:

At 500 mg/kg, 2/5 females died. At 750 mg/kg, 3/5 females died. At 1000 and 2500 mg/kg, 4/5 females died. At 3750 mg/kg, 5/5 females died. At 5000 mg/kg, 2/5 males and 4/5 females died. The LD₅₀ for males was reported to be > 5000 mg/kg and the LD₅₀ was for females reported to be 487 (188 to 1259) mg/kg.

Toxic symptoms included hypoactivity, stains around mouth, dyspnea, wheezing, compound discharge from mouth, ataxia, ptosis, body tremors, apparent blood discharge from anus, soft feces, hypotonia, tonic convulsions, salivation, chromorhinorrhea, hypothermia, prostration, and clonic convulsions. Gross necropsy revealed red diffuse lesions on lungs.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category II - WARNING.

(2) Acute Dermal Toxicity Study: Ciba-Geigy Pharmaceuticals Division; Report No. 289-84; January 2, 1985.

PROCEDURE:

Five male and five female New Zealand White rabbits were clipped and 24 hours later a single dose of 2010 mg/kg was applied under occlusive wrap to a test site on each animal. After 24 hours, the wrap was removed and test sites were washed and dried. Animals were observed frequently on the day of dosing and twice daily on days 2 through 14.

RESULTS:

No deaths occurred. No toxic symptoms were noted. The LD₅₀ was reported to be > 2010 mg/kg. No abnormalities were noted at gross necropsy.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(3) Acute Inhalation Toxicity Study: Ciba-Geigy Pharmaceuticals Division; Report No. 84296; April 18, 1985.

PROCEDURE:

Four groups each consisting of 5 male and 5 female Sprague-Dawley rats were exposed in a 200-liter stainless steel whole-body exposure chamber for 4 hours to one of the following the gravimetrically measured average chamber concentrations of test material: 2.3, 1.1, 0.34, or 0.07 rg/L. A control group of 5 males and 5 females were exposed to room air under similar conditions. Chamber concentration and particle

006195

size were measured hourly. After exposure, observations were conducted daily for 14 days. Gross necropsy was performed on all animals.

RESULTS:

At 2.3 and 1.1 mg/L, all animals died. At 0.34 mg/L, 1/5 males and 3/5 females died. At 0.07 mg/L, 1/5 males and 1/5 females died. The LC₅₀ for males was reported to be 0.33 (0.12 to 0.93) mg/L. The LC₅₀ for females was reported to be 0.20 (0.08 to 0.48) mg/L.

Toxic symptoms included dyspnea, gasping, lacrimation, chromodacryorrhea, pollakiuria, rasping, salivation, and soft stool. Gross necropsy revealed distended kidneys, stones in urinary bladder, protrusion on liver, mottled or red lungs, and enlarged fluid filled kidneys.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category II - WARNING.

(4) Primary Eye Irritation Study: Ciba-Geigy Pharmaceuticals Division; Report 294-84; February 6, 1985.

PROCEDURE:

Nine albino rabbits each received 100 mg of test material in the lower conjunctival sac of the right eye which was held shut for 1 second. The treated eyes of 3/9 animals were washed with tap water for 30 seconds. The remaining six animals' eyes were washed after 24 hours. Eye irritation was scored and eyes were examined using fluorescein stain.

RESULTS:

Eye irritation in the washed group was scored as follows: at 24 hours, corneal opacity (3/6 = 20); iris irritation (3/6 = 5); conjunctivae redness (2/3 = 2, 1/3 = 1), chemosis (1/3 = 3, 2/3 = 2) and discharge (2/3 = 2, 1/3 = 1); at 7 days, corneal opacity (1/3 = 60, 2/3 = 40), iris irritation (1/3 = 5, 1/3 - iris not discernible); conjunctivae redness (1/3 = 3, 1/3 = 2, 1/3 = 1), chemosis (1/3 = 3, 2/3 = 1) and discharge 1/3 = 2, 2/3 = 1); at 14 days, corneal opacity (1/3 = 80, 2/3 = 20), iris irritation (1/3 - iris not discernible), conjunctivae redness (2/3 = 1), chemosis (1/3 = 1), and discharge (2/3 = 1); at 21 days, corneal opacity (1/3 = 80, 2/3 = 20).

4

006192

At 24 hours after exposure, the entire corneal surface was stained in 3/3 animals when treated with fluorescein stain.

Eye irritation in the unwashed group was scored as follows: at 24 hours, corneal opacity (1/6 = 40, 5/6 = 20), iris irritation (6/6 = 5), conjunctivae redness (1/6 = 3), 5/6 = 2), chemosis (5/6 = 3, 1/6 = 2) and discharge (6/6 = 1); at 7 days, corneal opacity (3/6 = 60, 2/6 = 40, 1/6 = 20), iris irritation (3/6 - iris not discernable, 1/6 = 5), conjunctivae redness (1/6 = 3, 5/6 = 2), chemosis (2/6 = 2, 4/6 = 1) and discharge (5/6 = 1); at 14 days, corneal opacity (2/6 = 80, 2/6 = 60, 1/6 = 40), iris irritation (4/6 - iris not discernable, 1/6 = 5), conjunctivae redness (6/6 = 1), chemosis (1/6 = 2, 2/6 = 1) and discharge (3/6 = 1) and at 21 days, corneal opacity (3/6 = 80, 1/6 = 60, 1/6 = 40), iris irritation (4/6 - iris not discernable), conjunctivae redness (3/6 = 1), chemosis (1/6 = 2, 1/6 = 1) and discharge (1/6 = 1). At 24 hours, the entire corneal surface in 6/6 animals was stained when treated with fluorescein solution.

Other toxic symptoms which continued past day 21 included neovascularization, pannus, enophthalmus, and necrotic area(s) present on the eyelids and nictitating membrane.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category I - DANGER.

(5) Primary Skin Irritation Study: Ciba-Geigy Pharmaceuticals Division; Report No. 282-84; December 26, 1984.

PROCEDURE:

Six New Zealand White rabbits were shaved and approximately 24 hours later 0.5 gm of moistened test material was applied to one test site under occlusive wrap on each animal for 4 hours. After exposure, the test site was wiped clean with a moist paper towel. Animals were observed for 3 days and skin irritation was scored.

RESULTS:

No irritation was noted at 30 minutes or 24, 48, and 72 hours after exposure.

STUDY CLASSIFICATION: Core Guideline Data.

5

TOXICITY CATEGORY: Category IV.

(6) Dermal Sensitization Study: Ciba-Geigy Pharmaceuticals Division; Report No. 300-84; February 8, 1985.

PROCEDURE:

Two groups consisting of 10 guinea pigs were shaved and each received topical induction treatments under occlusive wrap on days 1, 3, 6, 8, 10, 13, 15, 17, 20, and 22 for 6 hours of exposure/application as follows: 0.5 g of test material moistened with purified water or 0.5 ml of 0.05% of 1-chloro-2,4-dinitro benzene (CDNB). Two weeks later, a dose identical to the induction treatment was administered to each group. One additional group of 10 animals was challenged with an identical application of test material and another group of 10 animals was challenged with an identical application of CDNB. Animals were observed once daily for physical appearance. Dermal observations were made prior to dosing on day 1, 24 hours after each induction treatment, and 24 and 48 hours after the challenge dose.

RESULTS:

One animal in the sensitized control group died. The sensitized control group exhibited dry flaky skin beginning on day 21 and scabbing at the test sites on day 23. After administration of the challenge dose, the nonsensitized control group exhibited no irritation and 8/9 animals in the sensitized control group exhibited mild erythema.

The sensitized test group exhibited dry flaky skin beginning on day 7 and continuing through day 23. Neither the sensitized nor nonsensitized test group exhibited skin irritation after treatment with the challenge dose.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Nonsensitizer.

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Pages _____ through _____ are not included.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
- ☐ Identity of product impurities.
- ☐ Description of the product manufacturing process.
- ☐ Description of quality control procedures.
- ☐ Identity of the source of product ingredients.
- ☐ Sales or other commercial/financial information.
- ☒ A draft product label.
- ☐ The product confidential statement of formula.
- ☐ Information about a pending registration action.
- ☐ FIFRA registration data.
- ☐ The document is a duplicate of page(s) _____.
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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.